Chronic Abdominal Pain in IBD

Request for Proposals (RFP)

Program Guidelines & Policies

Effective June 10, 2021

Crohn's & Colitis Foundation
National Office
Research Department
733 Third Avenue
Suite 510
New York, NY 10017

Contact:

Dr. Andrés Hurtado-Lorenzo, Vice President of Translational Research
Email: ahurtadolorenzo@crohnscolitisfoundation.org

Dr. Gerard Honig, Director of Research Innovation
Email: ghonig@crohnscolitisfoundation.org

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Key Dates

RFP Announcement	**June 10, 2021**
LOI Application deadline	**July 22, 2021**
Notification to submit full proposal	**August 6, 2021**
Full proposal deadline	**October 1, 2021**
Notification of award	**January 2021**

1. Overview

The Crohn's & Colitis Foundation (Foundation) is dedicated to addressing unmet needs of patients with inflammatory bowel diseases (IBD). The goal of this Request for Proposals (RFP) is to support research to advance the understanding of phenotypic heterogeneity and underlying biological mechanisms of chronic abdominal pain in IBD, as an approach towards improved management of this critical problem for which current treatments are inadequate.

Abdominal pain in patients with IBD is a common symptom which often resolves when an underlying inflammatory or obstructive condition has been addressed. However, many patients with IBD experience chronic abdominal pain which can persist even in the absence of overt inflammation. This can lead to impaired quality of life and in some cases disability. Current treatments are inadequate and present significant risk. Therefore, the development of new treatment modalities to effectively manage chronic abdominal pain in IBD is a pressing priority. Progress in this field has been limited by insufficient understanding of the diverse biological mechanisms of chronic abdominal pain in IBD, and how they relate to its heterogenous clinical manifestations.

Given this need, the Foundation convened a multidisciplinary workshop to identify knowledge gaps and strategies to move the field forward regarding both the understanding of the biology of chronic abdominal pain in IBD and its clinical management. The main immediate challenges identified were: (1) categorization of the heterogeneity of clinical presentations and underlying biological mechanisms to enable the discovery of novel therapeutic targets and biomarkers; (2) translationally relevant experimental models; (3) systems-level understanding of pain physiology, cell-cell interactions and triggers; and (4) identification of therapeutic mechanisms and novel targets within specific patient populations. This RFP, informed by the workshop outcomes, aims to improve the mechanistic and clinical understanding of chronic abdominal pain as experienced by IBD patients.

For further information on the background, goals and priorities of this RFP, refer to the Foundation's recent publication:
Hurtado-Lorenzo, Honig, Weaver, Larkin & Heller. Chronic Abdominal Pain in IBD Research Initiative: Unraveling Biological Mechanisms and Patient Heterogeneity to Personalize Treatment and Improve Clinical Outcomes. *Crohn's & Colitis 360.* In press.

2. Scope

Successful proposals must incorporate both of the following objectives:

1) *Characterization of the phenotypic and endotypic heterogeneity of IBD patients with chronic abdominal pain.* Study of how pain presents clinically and of the relevant molecular and physiological processes associated with the pain phenotypes is required. This is intended to enable identification of subgroups of patients, based on the underlying biological pathways (endotype) driving the different chronic pain clinical presentations (phenotype).

2) *Understanding mechanisms driving chronic pain in IBD*. A reverse translation approach, through which mechanistic hypotheses to be tested are grounded in patient-derived data and observations, is required. The ultimate goal should be the identification of potential therapeutic mechanisms for improved management of chronic pain in IBD within an identifiable patient subgroup with a specific pain endotype.

Characterization of pain phenotypes: A detailed definition and description of how pain manifests in the clinic in one or more cohorts of well-phenotyped IBD patients is required. Types of data to be collected may include, but are not limited to: response to different types of therapy; chronicity and periodicity; intensity; presence of other symptoms (e.g., fatigue) or psychiatric comorbidities (e.g., depression); secondary hyperalgesia; etc. Retrospective and/or prospective cohort studies will be considered. Inclusion of appropriate control group(s), such as IBD patients who experience acute pain but do not transition to chronic pain, is encouraged.

Characterization of pain endotypes: Multi-omics approaches to advance understanding of molecular and physiological processes within IBD patients suffering from chronic pain will be considered. The focus should be to characterize distinct molecular, cellular, immunological, microbial, and neurophysiological mechanisms relevant in patients suffering chronic abdominal pain, with the potential to stratify patients into subgroups based on the relevant mechanistic drivers of pain (endotypes). Potential approaches could include genomics, transcriptomics, microbiomics, metabolomics, physiological measures and brainomics (e.g., multimodal brain imaging). The goal is to identify endotypic biomarkers that can help stratify patients into different subgroups based on the biological pathways underlying the clinical presentation. This is ultimately intended to support novel precision medicine approaches for treatment of chronic pain. These studies should also advance understanding of the diverse biological mechanisms that can lead to persistent pain even during periods of remission.

Diverse patient cohort studies that correlate endotype-phenotype and environmental triggers are encouraged. Preliminary data to support the proposed research will be required.

Applicants are encouraged to consider the IBD Plexus® Academic RFP (https://www.crohnscolitisfoundation.org/research/grants-fellowships/ibd-plexus#rfp) as a potential supplemental source of data & samples from IBD patients.

Mechanistic studies: These studies should be based on the development or use of appropriate translationally relevant experimental models to accurately evaluate the mechanisms proposed to drive different pain endotypes. For preclinical models, consideration should be given towards recapitulating, within the limitations of preclinical systems, the chronicity and heterogeneity of pain phenotypes in IBD. Animal models will be considered, but also *in vitro* and *ex vivo* models, such as those derived from IBD patients' biological materials (e.g., biopsy supernatants, organoids); and humanized animal models. Projects that combine two or more methodological approaches will be preferred; for example, tissue-based or organoids-based in vitro studies; electrophysiology, optogenetics, visceral hypersensitivity in vivo studies and ex-vivo multi-omics studies. Projects that investigate neuro-immune mechanisms (peripheral and/or central) and central mechanisms of chronic pain in IBD are also encouraged.

Preclinical studies of potential therapeutic interventions and their mechanisms of action will also be considered and can include genetic or pharmacological manipulation of targets like ion channels, transporters, enzymes or secreted factors. Physiological interventions such as neuromodulation or neurostimulation will also be considered, in which case studies of the relevant therapeutic mechanisms are encouraged. **Because the goal of this RFP is to match this mechanistic research to the heterogeneous biology and phenotype of IBD patients who undergo chronic pain even during remission, priority will be given to study of pathways with demonstrated link to chronic abdominal pain in IBD patients (for example, alteration of the given target/pathway in patient samples or brain circuitry).**

Priority topics for mechanistic studies may include understanding of central and/or peripheral mechanisms of pain sensitization; microbiome factors; interactions between different types of cells involved in pain (e.g., between the microbiome, epithelial cells, neurons, immune cells etc.); understanding of the role of neuro-immune interactions and relevant environmental triggers. Ultimately, the goal should be to identify candidate central and/or peripheral nociceptive pathways that are altered in IBD patients and test causality in translationally relevant models to define the pathological mechanism of IBD-associated chronic pain in patient subgroups.

3. Eligibility

Applications from a team with the relevant expertise is required, with one lead Principal Investigator (PI) and at least one Co-PI.

- PI must be a senior faculty member (Professor, Head of Research, Associate Professor, etc.) with relevant expertise. Pain experts in other therapeutic areas are encouraged to apply in collaboration with co-investigators with expertise in IBD research.
- Applications from multiple co-investigator PIs (co-PIs) are encouraged. At least one co-PI must be a junior Co-PI (Instructor or Assistant Professor, prior to receiving an independent RO1 grant or international equivalent) with experience in IBD research and who is committed to pursue a career in IBD research as a part of his or her career development. Generally, junior Co-PI candidates should not be more than ten years beyond the attainment of their doctoral degree at the time of application.
- PI and Co-PIs must be employed by an institution (public non-profit, private non-profit, or government) engaged in health care and/or health related research. Collaborations of lead PI with subcontracted for-profit organizations are eligible. International applicants are also eligible to apply and there are no geographical restrictions regarding research site location(s).
- **If PI and/or junior co-PI are not primarily focused on pain research, the team must include an additional co-PI who is a scientist with proven track record in pain research.**
- Applications are strongly encouraged from diverse teams of applicants that include women, underrepresented racial and ethnic groups, individuals with disabilities, and/or individuals from disadvantaged backgrounds.

4. Grant Terms

Awards will be granted for 3 years with a maximum amount of $300,000 per year per project, for a total maximum budget of $900,00 per project, inclusive of all indirect expenses. It is anticipated that the Foundation will support up to 2 projects. The proposal can be submitted by a multi-center consortium or by an individual research group; one institution should be identified as the primary applicant and will be expected to manage subawards to other institutions, if any. Milestones will be agreed upon prior to project onset, and continued funding in years 2 and 3 is dependent on acceptable reasonable progress towards specified milestones. Indirect expenses must not exceed 10%.

5. How to apply

The investigators should submit the LOI by the specified deadline (see *Key Dates,* above). The LOIs will be evaluated competitively based on the alignment of the proposed study with the scope of the program and the feasibility of success of the study, as described in more detail in Appendix A (below). Only investigators who submitted an LOI and were invited to submit a full proposal are eligible to apply.

The investigators should provide a full research proposal and the accompanying document by the application deadline (see *Key Dates*, above) and according to the guidelines for proposal preparation and electronic submission (Appendix B, below).

All applications should be submitted through the proposalCENTRAL portal at the following URL: https://proposalcentral.altum.com/
Please refer to **Appendices A and B** for complete instructions of the application process.

6. Application Review and Selection Criteria

The proposals will undergo peer review by a multidisciplinary review committee and evaluated based on the following criteria:

The scope: The proposed study should align with the scope of the Chronic Pain in IBD RFP (section 2)

a. IBD patient-based studies to categorize phenotypic and endotypic heterogeneity of patients with chronic pain
b. Preclinical mechanistic studies in which, hypothesis is derived from patient-based data and observations, to better understand the biological drivers of pain chronicity
c. Experimental humanized in vitro and/or in vivo model-based preclinical studies to identify biological pathways and mechanisms of persistent visceral hypersensitivity
d. Studies must integrate both patient-based profiling and experimental models-based mechanistic studies.

Clinical and translational relevance to IBD: The central hypothesis and the aim should be based on an established link to chronic pain in IBD or have strong rationale for a novel IBD-related study in patients with IBD, and experimental models of pain ideally integrating humanized models. Translational potential of the study to impact the quality of life of IBD patients living with chronic pain will be assessed.

Research strategy: The proposal should demonstrate high feasibility and should have a reverse translational approach (bedside-to-bench), which is relevant for clinical application, sufficient preliminary data, well defined specific aims, clear experimental design, and contingency strategies. The proposal must be well written and understandable by the scientific audience. The lay summary must clearly summarize the proposal and be understandable for non-scientific reviewers. (**Note*:*** scoring of the proposal by the non-scientific patient reviewer will depend on his/her understanding of a well written lay summary. A poorly written lay summary will negatively impact the score provided by the patient reviewer).

Research team & environment: The factors to be considered are complementary expertise of the PIs and the collaborators, personnel expertise to carry out the aims of the research project, and suitable environment with infrastructure and organizational resources that would be required to perform the research. The senior investigator must show a successful track record in acquiring funding and published research in the field of pain research and/or IBD. The junior investigator should be on the clear trajectory for and have prior accomplishments required to becoming an independent investigator in the field of IBD and/or IBD pain. If PI and junior co-PI are not full-time pain researchers, the team must include an additional co-PI who is a scientist with proven record of a career devoted to pain research in IBD or another therapeutic area.

7. Reporting

Oversight and progress reports

The funded investigators will be required to submit a progress report via proposalCentral using the Foundation's progress report template. In addition to the progress report, as PI, you will be expected to present progress in oral presentations, including:

a. Teleconference with Foundation staff during the first and third quarter of the project year.
b. Mid-year oversight teleconference with Foundation staff and members of the relevant oversight committee.
c. Research Initiatives oversight meeting, including all Research Initiatives PIs and members of the oversight committees, to held virtually at the conclusion of each project year.

Intellectual property

The Foundation requires notification of any intellectual property (IP) arising out of or resulting from this scientific proposal within 30 days of receiving an invention disclosure or other notice indicating existence of intellectual property. Grantee shall provide the Foundation with written

notice, via proposalCentral, of all inventions and patents as required by the Foundation Patent and Intellectual Property Policy (Appendix C). Upon accepting the award and signifying this Grant Agreement, both Principal Investigator and Authorized Institutional Officer express agreement and compliance with the terms of the Foundation Patent and Intellectual Property Policy.

Additional award requirements
Funded investigators will be expected to submit financial reports and to report project outcomes using the ResearchFish portal. For additional information regarding the Foundation's post-award policies, including reporting, please refer to the Foundation's website:
https://www.crohnscolitisfoundation.org/research/post-award-policies

10. Contact Information

For more information and questions please contact Drs. Andrés Hurtado-Lorenzo and Gerard Honig at:
ahurtadolorenzo@crohnscolitisfoundation.com and ghonig@crohnscolitisfoundation.org

APPENDIX A: Letter of Intent (LOI) Submission Guidelines\

Before submitting the LOI, please read the Crohn's and Colitis Foundation's *Chronic Abdominal Pain in IBD* Request for Proposals (RFP) guidelines to ensure that the proposed study matches the scope of the program and that the applicant team and organization(s) meets the eligibility criteria.

The LOI should be submitted electronically on proposalCENTRAL by **July 22, 2021**. The LOI electronic submission form will include the following fields:

Title (100 characters limit)

Priority area and relevance to IBD (2500 characters limit): State, what population of IBD patients the study will potently benefit (Crohn's disease/ Ulcerative colitis). Explain the relevance of the main objective of the study for the IBD field and the scope of the Chronic Abdominal Pain in IBD RFP (See Section 2). Explain how the proposed study is aligned with the focus areas of 2019 Challenges in IBD research.

Total Budget: State the total requested budget for the proposed study. Estimate is acceptable and may be revised if a full proposal is submitted.

Primary Investigator (PI) and Institution, as defined by the primary performance site and the primary point of contact for budget management, and for research progress and financial reporting.

Co-PI and Other Key Personnel: If the primary PI is a junior investigator the co-PI should be a senior faculty member and primary investigator in an NIH-funded laboratory (or national equivalent funding agency for international applicants). **If PI and junior co-PI are not full-time pain researchers, the team must include an additional co-PI who is a scientist with proven record of a career devoted to pain research in IBD or another therapeutic area.**

Abstract (2500 characters limit): Briefly describe the main goal or the problem that the study will address, state hypothesis (if applicable), specific aims, research approach (including preliminary data), types of samples and/or the model methods that will be used, expected outcomes and the translational potential of the study. Please clearly state how the proposed study aligns with the scope of the Chronic Abdominal Pain in IBD RFP.

Scientific rationale and research plan: This section should provide a clear concise overview of the proposed work, including the background, objective, or hypothesis, its supporting rationale, specific aims, and proposed methodology. Space limit 3 pages (12,000 characters). It should include both from the two categories below:

a. Patient-based retrospective/prospective studies to define phenotypic and endotypic heterogeneity of IBD patients with chronic abdominal pain
b. Preclinical model-based studies to identify mechanisms of chronic abdominal pain, in which hypotheses are derived from data and/or observations in IBD patients

Research team (1000 characters limit): Briefly describe your team and explain how the PI's and the co-PI's expertise will contribute to the successful performance of the proposed work. Explain which team members meet the criteria in the RFP (e.g. junior Co-PI, established pain researcher, etc.)

PDF Attachments:

a. NIH Biosketches for key personnel (required)
b. References cited in application (optional)

c. Publications (optional)
d. Other Supplemental Information (optional)

Selection criteria

Reviewers of LOIs are asked to comment on the following selection criteria:

a. Alignment of the proposed study to the scope of the Chronic Abdominal Pain in IBD RFP and with the 2019 *Challenges in IBD Research* publication

b. Scientific strength of research proposal, rationale, specific aims and methodology

c. Study approach: integrating patient-based retrospective or prospective studies and preclinical studies using humanized models (*in vitro and/or in vivo and /or ex vivo)*

d. Strength of the scientific team, research environment and resources

e. Translational potential of the study to impact the quality of life of IBD patients living with chronic abdominal pain

APPENDIX B: Full Application Submission Guidelines

General information
The full application is due on **October 1, 2021.**
The application should be submitted to proposalCENTRAL at: https://proposalcentral.altum.com

Paper copies of the application are not accepted.

a. If you are a first-time user, register by clicking on "First time user." This will generate a confirmation number, which will be emailed to the email connected to this account. Confirm your registration by submitting this number when prompted.
b. Once you are a registered user, please click on "Grant opportunities" on the far right of the page and select Crohn's & Colitis Foundation under "Filter by Grant Maker" drop down menu on the upper left of the page.
c. Locate the "Chronic Pain in IBD" announcement and click "Apply now".
d. To activate the navigation bar on the left, enter the title of your proposal on the title page and "save" the application. The navigation bar on the left will now become interactive for you to continue your application.
e. Once completed, please validate and submit the application.

The Full Application form will include the following fields:
Title Page: Enter your title and "save" the application
Templates and Instructions: PI Biosketch and a New Vendor Form are available for download.
New Vendor Form *Required (part of Attachments section): Complete this form to authorize your institution to receive payment from the Foundation. This document contains the instruction on how payment will be transferred to your institution and should not include information on the Investigator. This is required even if institution has received Foundation funding in the past.
Enable other Users to Access the Proposal: Add personnel that can have access to review and edit the proposal.
Applicant /PI: Principal Investigator (PI) is defined as the one person responsible to report to the Foundation for scientific and technical direction of the project. Although Co-PI is required, only one person can be indicated as the main point of contact. Note: If the research (entirely or partially) is to be conducted in the Co-PI's laboratory, a subcontract budget needs to be proposed.
Institution and Contacts: Provide contact information of the signing staff officials at the institution where the lead PI is located and where the study will take place.
Co-PI(s), Collaborator and Key Personnel: Add the roles and the contact information for Co-Principal Investigator (Co-PI) and key personnel whom you would like to include on this application. Effort: Percentage Estimation of Amount of Time Allocated to this Project: Describe how the time (in percentages of full-time effort) is allocated in your current position at this institution.
Summary
Lay Summary
The Foundation has instituted a Stakeholder Reviewer Program, in which selected lay patients or caregivers participate as voting members of the various review committees. The Lay Summary

should provide a clear, concise overview, in a lay language, of the proposed work, including the main goal(s) or the central hypothesis of the study, the aims, the relevance to IBD and the alignment of the study with Challenges in IBD; In addition, please provide a brief impact statement describing the potential of the study to impact IBD research and/or healthcare; explain how the results of the study will potentially provide a novel solution or improve the current practices in IBD healthcare and disease management. Also include a brief glossary of any scientific terms included in your lay summary.
Please note that a lay summary that is not clearly written using lay language could affect the score provided by the Stakeholder Reviewer.

Scientific Summary of the Project
The Scientific Summary should provide a clear, concise overview of the proposed work, including the background, objective(s), specific aims, research approach (including preliminary studies, if available, types of samples and/or the model methods that will be used), expected outcomes and the translational potential of the study. Please include references and upload a Cited References document as an attachment.
Relevance to IBD:
Re-state, what population of IBD patients the study will potently benefit (Crohn's disease/ Ulcerative colitis). Explain the relevance of the main objective of the study for the IBD field. Explain how the proposed study is aligned with the scope of this RFP.

Budget Period Detail

Start and End Dates
Specify date on which you expect to start this project. Enter dates for 3 years in 1-year increments.
Complete the e-form total budget.
The budget requested per year may not exceed $300,000 inclusive of 10% indirect cost (Direct costs: $272,727; indirect costs: $27,273).

Budget Summary Detail: The total budget request for year 1 must not exceed $300,000 inclusive of 10% indirect cost. Salaries are capped at NIH limits. The total budget for 3 years is $900,000 inclusive of 10% indirect costs (Direct costs: $818,182; indirect costs: $81,818). Justification of the budget for the 3-year period must be provided.

Current and Pending Financial Support: Please provide information on additional ongoing funding that currently supports this research project.

Organization Assurance: Human/Animal Studies Approval/Recombinant DNA
All activities involving human subjects or vertebrate animals must be approved by an appropriate institutional review board (IRB/IACUC) or equivalent prior to the start date of award. Indicate with "Yes" or "No" response, and if yes indicate date of approval and attach approval in that Attachments Section.
Copies of the IRB approval should be provided to the Foundation's Research Department. If approval is not available at the time of application, provide a date of anticipated approval. **This approval must be received before the start date of the approved grant.**

Human and/or Animal Approvals: Upload IRB/IACUC approvals for human and animal research

Upload Attachments:

- **Cover page**
  Describe background and expertise of the PI, Co-PI and the relevant investigators, and the role/ tasks to be performed by each investigator
- **Research Plan/Protocol**

The description of the proposed research project must include the following items in sufficient detail to permit evaluation of the scientific merit of the study. This cannot exceed 10 pages, single spaced. The page limits distribution indicated below are included as a guideline and not required.

- Overall Objectives and specific aims (no more than 1 page)
  - Briefly outline the general scientific objectives
  - Describe concisely and realistically what the specific research described in this application is intended to accomplish. Specifically outline Aims for year 1, year 2 or year 3, goals, 6-month-interval milestones and timelines. State any hypotheses to be tested.
- Background -including preliminary data (no more than 3 pages)
  - Outline the previous work in the area by others, and the preliminary data or previous studies by the investigator(s). Enough preliminary data should be included in the application to demonstrate that the project is feasible, and that the investigator is likely to complete the project successfully in the duration of the grant. Provide evidence that supports clinically relevant observations made in patients
- Detailed description of methods and materials to be used (no more than 5 pages)
  - Provide a detailed discussion of the experimental design, procedures, and materials to be used to accomplish the Specific Aims.
  - Describe protocols, including methods for new techniques, and explain the advantages over existing methodologies.
  - Discuss the kinds of data expected to be obtained and the means by which data will be analyzed and interpreted.
  - Justify the use of any animal models (i.e., choice of species, number used, etc.).
  - Discuss potential difficulties and/or limitations of the proposed procedures and alternative approaches to achieve aims.
- Significance and relevance of the proposed research to Crohn's disease and/or ulcerative colitis and to the Chronic Pain in IBD RFP (no more than 1 page).
  - Justify the significance of the results of this project to the understanding of the etiology, pathogenesis, therapy, and prevention of pain in IBD. Specifically identify the gaps this project is intended to fill related to the Chronic Pain in IBD RFP.
- Facilities Available to carry out the Proposed Studies (one or two paragraphs)
  - Describe the facilities available, including square footage, equipment, animal care facilities, and other environmental factors. Pay particular attention to those items required for successful completion of this proposal. Include a description for each facility to be involved.
- References (no more than 2 pages)

- Literature citations should be listed in this section, at the end of the Research Plan. ***These are not counted as part of the 10-page limit.

- **Biosketches for Key Personnel**
  - Biosketch (NIH format) for PI, Co-PI, and nutritional research expert (required), and additional key personnel (optional).
- **Letters of Collaboration**
  - Attach supporting letter(s)
- **References/ Appendices (optional)**
  - Uploaded reference material may include, but not limited to:
    a. Article references
    b. Abstracts
    c. Original Pictures
    d. Other Letters of Support

- **Signed Signature Pages**
  This document is generated by the PDFs and Signature Pages module after submitting all the forms and uploading all the required documents. Module PDFs and Signature Pages is located on the navigation bar on the left-hand side.
- **Timeline and Milestones**
  Timeline for completion of project (Gantt chart or similar format): List of milestones projected for every six months of the project period.

Validate: Click *Validate* to check for any missing REQUIRED information or files. All missing required information will be listed on the screen.

PDFs and Signature Pages

Click *Print Signature Pages* to be signed by the applicant and the organization officials. Upload the signed document on the Upload Attachments module.
Click *Print Signature Pages and Attached PFD Files* if you would like to save the full application for your records. Do not upload the full application with the signed signature pages in Upload Attachment module.

Submit

Only the primary PI is authorized to submit the application.

APPENDIX C: IP policy

All inventions or intellectual property ("Property") that results from research supported, in whole or in part, by grant awards from the Foundation must be reported in writing at the earliest possible time to Foundation. The grantee institution agrees to notify the Foundation within a reasonable time, preferably within 30 days, of receiving an invention disclosure or other notice indicating existence of a Property and to notify the Foundation immediately of the decision to apply for letters of patent or other legal protection for the Property. The Foundation agrees to keep all information confidential and not to release any information relating to such inventions, intellectual property or applications for protection to any third party, except as specifically set forth below or upon written agreement with the grantee institution, which consent cannot be unreasonably withheld. All patenting expenses or intellectual property application expenses shall be borne by the grantee institution.

Title to all Property shall reside with the grantee institution to the extent that such title is claimed by the institution under its institutional patent policy or procedure. If a grantee institution has no established institutional patent policy or procedure for administering inventions or intellectual property, or if the institutional patent policy or procedure does not claim rights for the institution or individual inventor, then Foundation shall have the right to determine the disposition of the Property rights in accordance with the provisions set forth below.

Distribution of income derived from any Property, which might include equity disposition, shall be shared by the grantee institution and the Foundation on mutually agreeable terms, such terms to be determined as soon as practicable, preferably prior to any licensing or commercial exploitation of the Property, and in any event no later than six months after first receipt of income. Such distribution shall be guided by the principle that the Foundation's proportion of the income shall be reasonably related to the Foundation's proportion of support for the research leading to the Property. The grantee institution agrees to notify the Foundation within a reasonable time of beginning negotiations with potential licensees and to notify the Foundation upon execution of any license or other agreement to commercialize the Property. The grantee institution will provide a copy of the license or other agreement, or an excerpt of the financial terms relevant to the Foundation's right to income from the Property together with the name of the licensee, the subject matter of the license and any other terms relevant to the foundation, including without limitation whether such license is exclusive or nonexclusive.

If any Property is made with or results from the joint support of the foundation and another organization, that organization, the grantee institution, and the Foundation will confer, in good faith, to arrive at a mutually satisfactory disposition of the Property rights guided by the principle that distributions of income be made in proportion to each party's contribution of support for the research leading to the Property.

No patent, patent application or other type of protection for a Property shall be abandoned without first notifying the Foundation and giving the Foundation a reasonable opportunity to take title to the Property.

If grantee institution does not effectuate a license to Property within four (4) years from the date that such Property is disclosed in writing through an invention disclosure or similar form to the grantee institution by the principal investigator, then the Foundation shall have the right to

introduce to the grantee institution one or more bona fide potential licensees and the grantee institution shall enter into good faith negotiations for license of the Property with such potential licensee(s). Upon consummation of any such license, the Foundation's introduction of the licensee to the grantee institution shall be counted to the benefit of the Foundation in calculating its share of any income from the Property.

The grantee institution agrees that when it licenses a Property, it will use reasonable efforts to obligate the licensee to exert its best efforts to commercialize or cause to be commercialized the Property as rapidly as practical, consistent with sound and reasonable business practices and judgment, and reserve the right to terminate the license upon a failure by licensee to do so. If the grantee institution relicenses any Property, the Foundation shall be entitled to a share of any relicensed Property income according to the principles set forth above.

The Foundation reserves the right to public acknowledgment for Property resulting from research supported by the Foundation. However, the Foundation's name and logo may not be used in association with any Property without the prior written approval of the Foundation.

The Foundation shall have use of the Property without payment of royalties or license fees solely for the use by the Foundation for its own intramural or public education purposes, but not for any of its grantee institutions.

Awardees and grantee institutions are responsible for ensuring that there are no inconsistencies in their consulting or business agreements that conflict with this policy